



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,909	07/21/2003	Eileen Tozer	D1410-2US	7087
29062 7590 06/25/2010 VERENIUM CORPORATION Intellectual Property Department P.O. Box 910550 SAN DIEGO, CA 92191-0550				
EXAMINER BERTAGNA, ANGELA MARIE				
ART UNIT		PAPER NUMBER		
1637				
NOTIFICATION DATE		DELIVERY MODE		
06/25/2010		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

lynn.linkowski@verenum.com

lp@verenum.com

greg.einhorn@verenum.com

Office Action Summary

Application No.

10/624,909

Applicant(s)

TOZER ET AL.

Examiner

Angela M. Bertagna

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☒ Claim(s) 189 is/are allowed.
- 6) ☒ Claim(s) 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 207, 217, 218 and 225-228 is/are rejected.
- 7) ☒ Claim(s) 188 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 July 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 1,14,15,35,42-45,48,49,87,111,113,116,138,143,174,175,177,182,184,187-190,207,208,217-229 and 231.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 42,111,113,116,138,143,174,175,177,182,184,187,190,208,219-224,229 and 231.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(c), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(c) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 19, 2010 has been entered.

Claims 1, 14, 15, 35, 42-45, 48, 49, 87, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187-190, 207, 208, 217-229, and 231 are currently pending. In the response, claims 1, 188, 218, and 225 were amended, and claims 33, 51, 54, 56, 58, 106, 107, 215, 216, and 230 were canceled. Claims 42, 106, 107, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187, 190, 208, 219-224, 229, and 231 remain withdrawn from consideration as being drawn to a non-elected invention.

The following include new and/or modified grounds of rejection. Any previously made objections or rejections not reiterated below have been withdrawn. Applicant's arguments filed on January 19, 2010 have been fully considered, but they were not persuasive to overcome all of the rejections.

Drawings

2. (A) Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and,

unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

In this case, the fee set forth in 37 CFR 1.17(h) has not been paid, and, accordingly, the color drawings filed on July 21, 2003 are objected to as the required petition under 37 CFR 1.84(a)(2) has not been granted.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637

(B) The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: **270 and 278 (see Figure 3)**. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

3. Claim 188 is objected to because of the following informalities: The status identifier of this claim is incorrect.

Claim Rejections - 35 USC § 112, 1st paragraph (Written Description)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 207, 217, 218, and 225-228 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.**

The central inquiry when considering written description is whether an ordinary artisan would reasonably conclude that Applicant was in possession of the claimed invention at the time of filing (see MPEP 2163 and *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1566-67, 43 USPQ2d 1398, 1404-05 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998)).

According to Revision I of the Written Description Training Materials (posted 4/11/08 at <http://www.uspto.gov/web/menu/written/pdf>), the following factors should be considered, when

evaluating a claim for compliance with the written description requirement: (a) actual reduction to practice, (b) disclosure of drawings or structural chemical formulas (c) sufficient relevant identifying characteristics (d) method of making the claimed invention, (e) level of skill and knowledge in the art, and (f) predictability in the art (see page 1 of the Training Materials).

The instant claims are drawn to isolated nucleic acids that encode a fluorescent polypeptide and are at least 95%, 97%, or 98% identical to SEQ ID NO: 29 and compositions, specifically vectors and transformed cells, comprising said nucleic acids. The genus of nucleic acids having at least 95%, 97%, or 98% identity to SEQ ID NO: 29 is very large and includes hundreds of thousands of structurally distinct molecules, each of which may encode a polypeptide having different functional properties. The claims limit this large genus to nucleic acids that encode a fluorescent protein.

The specification teaches the nucleic acid sequence of SEQ ID NO: 29 (see page 17 of the Sequence Listing and page 37), and therefore, it contains an actual reduction to practice of one member within the claimed genus. The specification also discloses a nucleic acid that is at least 95% identical to SEQ ID NO: 29 and encodes a fluorescent protein (see Table 2 on page 124, where SEQ ID NO: 17, which is 99% identical to SEQ ID NO: 29 is taught). However, none of the other fluorescent proteins described in Table 2 on pages 124-125 of the specification fall within the claimed genus of nucleic acids. Also, neither the specification nor the prior art describes the regions of SEQ ID NO: 29 and those sequences at least 95% identical thereto that are critical for conferring fluorescence activity to the encoded protein, for example, by mutagenesis analysis, sequence analysis, or other methods. The claimed nucleic acids also do not share a high degree of similarity to other known fluorescent proteins, and, as a result, it is not

clear that the information available in the art concerning function-critical regions of other fluorescent proteins, such as GFP, would be applicable to the proteins encoded by the claimed nucleic acids. Furthermore, as evidenced by the specification of the instant application at page 129, for example, there is a high degree of unpredictability in the art regarding structure-function correlations, and even a single nucleotide substitution can abolish the function of the protein encoded by a mutant nucleic acid. Accordingly, the level of skill required in this unpredictable art is high. As a result, the specification clearly fails to adequately describe the relevant identifying characteristics that are critical for determining whether a particular nucleic acid with the claimed genera of nucleic acids having at least 95%, at least 97%, or at least 98% identity to SEQ ID NO: 29 also possesses the required functional property of fluorescence. In the absence of such disclosure, it must be concluded that Applicant was not in possession of the claimed invention at the time of filing. Accordingly, claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 207, 217, 218, and 225-228 have been rejected under 35 U.S.C. 112, first paragraph for failing to comply with the written description requirement.

Claim Rejections - 35 USC § 112, 1st paragraph (Scope of Enablement)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 207, 217, 218, and 225-228 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid that encodes a fluorescent protein and comprises SEQ ID NO: 29 or SEQ

ID NO: 17, does not reasonably provide enablement for any other nucleic acids that are at least 95% identical to SEQ ID NO: 29 and that encode a fluorescent protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Nature of the Invention & Breadth of the Claims

The instant claims are drawn to isolated nucleic acids that encode a fluorescent polypeptide and are at least 95%, 97% or 98% identical to SEQ ID NO: 29 and compositions, specifically vectors and transformed cells, comprising said nucleic acids. The genus of nucleic acids having at least 95%, 97%, or 98% identity to SEQ ID NO: 29 is very large and includes hundreds of thousands of structurally distinct molecules, each of which may encode a polypeptide having different functional properties. The claims limit this large genus to nucleic acids that encode a fluorescent protein.

Guidance in the Specification and Working Examples

The specification teaches the nucleic acid sequence of SEQ ID NO: 29 (see page 17 of the Sequence Listing and page 37), and, therefore, it contains an actual reduction to practice of one member within the claimed genus. The specification also discloses a nucleic acid that is at least 95% identical to SEQ ID NO: 29 and encodes a fluorescent protein (see Table 2 on page 124, where SEQ ID NO: 17, which is 99% identical to SEQ ID NO: 29 is taught). However, none of the other fluorescent proteins described in Table 2 on pages 124-125 of the specification fall within the claimed genus of nucleic acids. Also, neither the specification nor the prior art describes the regions of SEQ ID NO: 29 and those sequences at least 95% identical thereto that are critical for conferring fluorescence activity to the encoded protein, for example, by mutagenesis analysis, sequence analysis, or other methods.

The working examples (see pages 155-159) also do not describe the regions of the disclosed nucleic acids that are critical for encoding a functional (*i.e.*, fluorescent) protein. In Example 1 cDNA libraries prepared from marine sources were analyzed to identify cDNA clones encoding fluorescent proteins (see pages 155-156). In Example 2 (see pages 156-158), fluorescent proteins were isolated and purified. In Example 3 (see pages 158-159), the excitation and emission properties for a subset of the disclosed fluorescent proteins was determined. However, Examples 1-3 do not provide any discussion of regions of the proteins that are required for fluorescence activity.

State of the Prior Art and Unpredictability

The prior art does not teach isolated nucleic acids that are at least 95% identical to SEQ ID NO: 29 and encode a fluorescent polypeptide, and, therefore, the prior art does not identify the regions of the claimed nucleic acids that are critical for fluorescence activity. The claimed nucleic acids also do not show a significant level of similarity to other fluorescent proteins known in the art, and, as a result, it is not clear that the information available in the art concerning function-critical regions of other fluorescent proteins, such as GFP, would be applicable to the proteins encoded by the claimed nucleic acids. Furthermore, there is a high degree of unpredictability in the art regarding structure-function correlations, and it is well established that even a single nucleotide substitution can abolish the function of the protein encoded by the mutant nucleic acid (see page 129 of the specification, for example). Therefore, it is highly unpredictable as to whether a nucleic acid having at least 95% identity to SEQ ID NO: 29 will possess fluorescence activity, particularly since neither the specification nor the art teaches the regions of the protein that are critical for this activity.

Quantity of Experimentation

The quantity of experimentation required in this case is immense, because it would require significant study and experimentation to determine whether a nucleic acid having at least 95% identity to SEQ ID NO: 29 also encodes a fluorescent protein. Each different variant nucleic acid would have to be produced via mutagenesis, and the encoded proteins would have to be expressed and characterized functionally. In the absence of any guidance in the specification or the art regarding regions of SEQ ID NO: 29 that are critical for determining fluorescence

activity, the ordinary artisan would have little or no starting point for determining whether a given variant of SEQ ID NO: 29 encodes a fluorescent protein. Given the unpredictability in the art regarding the effect of nucleic acid mutations on the functionality of the proteins encoded therefrom, the ordinary artisan would be required to undertake this large quantity of experimentation with little or no guarantee of success.

The Level of skill in the art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the instant claims are broadly drawn to isolated nucleic acids having at least 95% identity to SEQ ID NO: 29 and that encode a fluorescent protein. Despite the breadth of the claims, the specification only teaches a small number of nucleic acids falling within the claimed genus and provides no guidance regarding the regions of SEQ ID NO: 29 that are required for the fluorescence activity of the claimed proteins. Thus, given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to determine those regions of SEQ ID NO: 29 required for fluorescence activity, the lack of guidance provided in the specification, balanced only against the high skill level in the art, it is the position of the examiner that the claimed nucleic acid products fail to comply with the enablement requirement.

Allowable Subject Matter

6. Claim 189 is allowed.

Response to Arguments

7. Applicant's arguments filed on January 19, 2010 have been fully considered, and they were persuasive in part.

Claim Objections

Applicant argues that the amendment has obviated the previously made objections to claims 33, 218, and 225 (see page 14). This argument was persuasive, and, accordingly, the objections have been withdrawn.

Rejection under 35 U.S.C. 102(b)

Applicant's arguments, see page 17, regarding the rejection of claim 33 under 35 U.S.C. 102(b) as being anticipated by Adams, have been fully considered and are persuasive. As noted by the Applicant at page 17, claim 33 has been canceled rendering the previous rejection moot. Accordingly, it has been withdrawn.

Rejection under 35 U.S.C. 112, first paragraph (written description)

Regarding the rejection of claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 207, 217, 218, and 225-228 under 35 U.S.C. 112, first paragraph (written description), Applicant argues that the claimed invention has been sufficiently described in the original disclosure (pages 14-15). In particular, Applicant argues that "[A]ll polynucleotides of the claimed invention are described by structure (the exemplary SEQ ID NO: 29), and physico-chemical property (polynucleotides

having at least 95% sequence identity to SEQ ID NO: 29), and a function (fluorescent polypeptide activity)", and that this description of a genus of polynucleotides satisfies the written description requirement of 35 U.S.C. 112, first paragraph (page 14). Applicant also argues that a description of the structural features in the claimed nucleic acids that correspond to the required functional property (fluorescence activity) is not necessary to fulfill the written description requirement, because the ordinary artisan would have been able to screen nucleic acids within the claimed genus for fluorescence activity using routine methods, such as those described in the specification (pages 14-15).

Applicant's arguments regarding the written description rejection have been fully considered, but they were not persuasive. In contrast to Applicant's arguments at page 14, all of the claimed nucleic acids have not been described with respect to their functional properties beyond a general assertion that any polynucleotide within the claimed genus will encode a fluorescent protein. Rather, only one protein encoded by a nucleic acid within the claimed genus has been described in terms of its functional properties (see Table 2 on pages 124-125). As discussed in the rejection, in the absence of a disclosure either in the original disclosure or in the prior art of the structural features that must be present for a nucleic acid within the claimed genus to encode a fluorescent protein, the claimed invention has not been adequately described, because the relevant identifying characteristics have not been identified.

Also, Applicant's argument that an explicit disclosure of the structural features of the claimed nucleic acids required for fluorescence activity is unnecessary, since the claimed nucleic acids could be easily screened for fluorescence activity (see pages 14-15) was unpersuasive, because the aforementioned structure-function correlation is absolutely critical for an adequate

disclosure of the relevant identifying characteristics of the claimed invention to exist. As discussed above, the claimed nucleic acids share little homology with known fluorescent proteins, and the disclosure provides absolutely no guidance concerning the regions of the encoded proteins that are critical for fluorescence activity. This lack of guidance in the art and original disclosure coupled with the inherent unpredictability in the art results in the ordinary artisan having no idea *a priori* as to which nucleic acids at least 95% identical to the claimed SEQ ID NO: 29 will possess the required functional property of encoding a fluorescent protein, and, therefore, a large portion of the thousands of different variants encompassed by the claims would have to be tested to identify the relevant identifying characteristics of the claimed invention. Thus, when the original disclosure is evaluated according to the guidelines set forth in the Written Description Training Materials, it is clear that the claimed genus of nucleic acids has not been adequately described.

Since Applicant's arguments were not persuasive, the rejection has been maintained with minor modifications.

Rejection under 35 U.S.C. 112, first paragraph (scope of enablement)

Applicant's arguments filed on January 19, 2010 remain pertinent to the new grounds of rejection above, where claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 207, 217, 218, and 225-228 have been rejected under 35 U.S.C. 112, first paragraph (scope of enablement). Applicant argues that the original disclosure provides sufficient detail concerning methods of making and using the claimed nucleic acid sequences to satisfy the enablement requirement and notes that the statements in the specification must be accorded appropriate weight unless there is an objective

reason to doubt the truth of the statements made therein (pages 15-16). Applicant also argues that methods of making variant nucleic acids, expressing recombinant proteins, and screening them for fluorescence activity were well-established in the art at the time of invention, and, therefore, only routine and predictable experimentation would be required of the ordinary artisan (pages 15-16). Applicant further notes that the quantity of experimentation alone cannot support an enablement rejection when the experimentation is routine (pages 15-16).

Applicant's arguments have been fully considered, but they were not persuasive, because, although methods of making mutations in nucleic acids, expressing recombinant proteins, and screening them for fluorescence activity were known in the art at the time of the invention, the lack of guidance in the disclosure and the art concerning the structural features of the claimed nucleic acids that are required for fluorescence activity in the resulting protein coupled with the inherent unpredictability associated with nucleic acid substitutions would result in the ordinary artisan having no starting point for screening nucleic acids within the claimed genus for the required functional activity. Rather, the ordinary artisan would have to conduct a large quantity of unpredictable experimentation to identify the regions of the claimed nucleic acids required for fluorescence activity to be present in the resulting proteins. Thus, the ordinary artisan would essentially be required to identify a critical feature of the claimed genus of nucleic acid products. This is considered to constitute undue experimentation.

Applicant's attention is also directed to MPEP 2164.03, which states, "The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is

predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability.....However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims....This is because it is not obvious from the disclosure of one species, what other species will work."

Also, as noted in MPEP 2144.06, "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976))."

In this case, as discussed above, by failing to identify the structural features that are correlated with the required function, neither the specification nor the prior art provides guidance as to the direction in which the experimentation should proceed. As a result, although the particular method steps (*i.e.*, site-directed mutagenesis, protein expression and purification, *etc*) could be readily conducted by the ordinary artisan, the ordinary artisan would have had to conduct this experimentation with essentially no starting point other than the disclosed nucleic acid sequences and would have had to identify the features of the claimed nucleic acids that are

required for fluorescence activity. Since this is a critical feature of the claimed invention, this undertaking would not be routine, but, rather, an inventive undertaking. The experimentation required of the ordinary artisan would also necessarily be associated with a high degree of unpredictability, since nucleic acid substitutions do not always have predictable consequences, particularly when, as in the instant case, they are made in a family nucleic acids that encode a relatively poorly characterized group of proteins. Accordingly, the full scope of the claimed genus of products is not enabled by the original disclosure. Since Applicant's arguments were not persuasive, the rejection has been maintained with minor modifications.

Conclusion

8. Claims 1, 14, 15, 35, 43-45, 48, 49, 87, 188, 217, 218, and 225-228 are free of the art, but they have been rejected for failing to comply with the requirements of 35 U.S.C. 112, first paragraph. Claim 189 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

Art Unit: 1637

applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Angela M Bertagna/
Examiner, Art Unit 1637